STATUS OF CLAIMS

Claims 1-37 are pending in the application. Claims 22-32 were withdrawn from consideration pursuant to a restriction requirement. Applicant has amended claim 1 and added new dependent claim 38. Support for new claim 38 is provided in original claim 5 as filed. Support for the amendment to claim 1 is provided in original claim 1 as filed. There is no issue of new matter.

REMARKS

Applicants acknowledge that pursuant to a December 21, 2007 Notice of Panel Decision from Pre-Appeal Brief Review, the Examiner has withdrawn the prior rejections under 35 U.S.C. § 112, first paragraph and 35 U.S.C. § 103(a). The Examiner has the following new rejections.

Rejection Under 35 U.S.C. § 102(b)

Claims 1-4, 6, 17, and 33-34 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Devane et al. (U.S. Pat. No. 6,228,398).

In response, Applicants respectfully traverse the rejections and their accompanying remarks. Devane et al. does not teach the invention of the claims. Specifically, Devane et al. fails to teach all of the elements of the present invention as claimed in amended independent claim 1, which is directed to an injectable or insertable ***solid or semi-solid dosage form for producing specific necrosis of tissue that comes into contact with the tissue*** comprising: a ***biodisintegrable binder*** and a ***chemical ablation agent in a concentration effective to cause necrosis of said tissue***, wherein said dosage form is a sterile, ***solid or semi-solid dosage form*** (emphasis added).

For a reference to anticipate a claim it must disclose ***each and every elemen***t of the claim. *See* MPEP 2131 and cases cited therein, *especially Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989) and *In re Marshall*, 578 F.2d 301, 304, 198 USPQ 344, 346 (Fed. Cir. 1978)(emphasis added).

The Devane et al. reference fails as an anticipatory reference because it fails to disclose all of the features of the claimed invention. For example, Devane et al. fails to teach

a solid or semi-solid dosage form for producing specific necrosis of tissue. Devane et al. fails to teach such dosage form that comprises a biodisintegrable binder and a chemical ablation agent in a solid or semi-solid form. Indeed, the term "necrosis" does not appear in Devane et al. The terms "ablation" or "chemical ablation agent" do not appear in Devane et al. The term "binder" or "biodisintegrable binder" doe not appear in Devane et al. Applicants state that these terms are missing because Devane et al. does not teach these claim features. Rather, Devane et al. discloses an oral controlled release composition that delivers active ingredients in a pulsatile manner. For example, Devane et al. discloses a "first population of active ingredient-containing particles" that constitutes an "immediate release component" and a "second population of active ingredient-containing particles that is coated with a "modified release coating" which "causes a lag time between the release of active ingredient from the first population of active ingredient containg [sic] particles and the release of active ingredient from the second population of active ingredient containing particles." (Devane et al., col. 4, lines 10-44).

Nowhere does Devane et al. teach a dosage form for producing specific necrosis of tissue. To address this deficiency, the Examiner states that "Devane et al. teach chemotherapeutic agents which are none [sic] in art of cancer therapy as agents which cause ablation and necrosis of infected or tumorous tissue." Applicants challenge such assertion and states that it is neither supported by Devane et al., nor evidenced by any Examiner. Applicants states that one of ordinary skill in the art would not equate a chemotherapeutic agent with a chemical ablation agent. The Examiner has not pointed out any specific chemotherapeutic agents disclosed by Devane et al., nor shown any evidence that such agents are chemical ablation agents.

Indeed, Applicants respectfully submit that it is implausible that the ***oral*** dosage forms of Devane et al. would produce the "specific necrosis of tissue that comes into contact with the tissue" as claimed since that would entail damaging the tissues of the oral cavity and oral passageways while orally ingesting the composition of Devane et al. Devane et al. is devoid of any reference to a chemical ablation agent. Rather, Devane et al. merely lists "chemotherapy agents" in a long list of potential "active ingredient[s] whose

pharmacological and/or therapeutic effects benefit from having a wash-out period between plasma concentration peaks, such as those active ingredients susceptible to the development of patient tolerance." (Devane et al., col. 6, lines 13-63). There is simply disclosure, enabling or otherwise, of a dosage form made of a chemical ablation agent that specifically necrotizes contact tissue. The Examiner has not shown otherwise.

Even if the oral dosage form of Devane et al. were somehow found to be possible to function as a dosage form for producing specific necrosis of tissue that comes into contact with the tissue, a holding of inherency must flow as a ***necessary*** conclusion from the prior art, not simply a possible one. The fact that a certain result or characteristic ***may*** occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 U.S.P.Q. 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745, 49 U.S.P.Q.2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted); MPEP 2112 IV.

The Examiner has provided no extrinsic evidence to make clear that a dosage form that specifically necrotizes tissue upon contact is ***necessarily present*** in the dosage forms of Devane et al. Thus, Applicants respectfully submit that inherency has not been shown and requests that the Examiner reconsider and withdraw the rejection under 35 U.S.C. 102(b).

In light of the above remarks, Applicants state that the rejection under 102(b) has been obviated and all outstanding issues have been resolved. Thus, reconsideration and withdrawal of this rejection under 35 U.S.C. 102(b) is respectfully requested.

Rejection Under 35 U.S.C. § 103(a)

Claims 7-16, 18-21, and 35-37 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,905,475 (Hauschild et al.) and U.S. Patent No. 7,015,253 (Escandon et al.), in view of U.S. Patent Nos. 5,469,854 (Unger I) and 5,733,572 (Unger II).

In response, Applicants respectfully traverse the rejection and its accompanying remarks. The rejection over Hauschild et al. and Escandon et al. in view of Unger I or Unger II is clearly erroneous because none of these references discloses the claimed injectable or insertable solid or semi-solid dosage form for producing specific necrosis of tissue that comes into contact with the tissue. Further, there is no suggestion in these references to modify the treatments or injections of these references to result in the pending claims, either singly or in combination nor is there any reasonable expectation of success that combining the teachings will result in the claimed dosage form.

Applicants also assert that the Examiner has failed to establish a *prima facie* case of obviousness. For a reference or combination of references to support a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion and/or motivation to make the necessary modification of the teaching of the reference or references combined to result in the pending claims; (2) there must be a reasonable expectation of success; and (3) the prior art reference must ***teach or suggest all the claim limitations***. MPEP § 2142-2143 (emphasis added); *see In re Jones*, 958 F.2d 347, 351, 21 U.S.P.Q.2d 1941, 1943-44 (Fed. Cir. 1992); *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q. 1596, 1598-99 (Fed. Cir. 1988).

It is respectfully submitted that the rejection based on these references is improper on its face. The Examiner has presented no reasoning to support a conclusion of obviousness for a solid or semi-solid dosage form with the recited biodisintegrable binder and chemical ablation agent. *See* MPEP § 706.02(j)(D) and the cases cited therein.

The cited references fail to teach all of the elements of the present invention as claimed in amended independent claim 1, which is directed to an injectable or insertable dosage form for producing specific necrosis of tissue that comes into contact with the tissue

comprising: a biodisintegrable binder and a chemical ablation agent in a concentration effective to cause necrosis of said tissue, wherein said dosage form is a sterile, solid or semi-solid dosage form.

Hauschild et al. discloses a syringe for injecting liquid ethanol into the prostate tissue. Specifically, Hauschild et al. discloses a "surgical instrument 20 for use in treating prostate tissue by injecting an effective amount of an active ingredient (e.g. ethanol, acetic acid, phenol, Lidocaine, bulking agents, botox, oxybutenin, carboxylic acid)." (Hauschild et al., col. 2, line 66 to col. 3, line 3). The invention of Hauschild et al., is a "surgical instrument" and as such, there is no disclosure of solid or semi-solid dosage form formulations of any type. Rather, Hauschild et al. teach the structure and mechanics of the surgical device and states that "[a] small volume…of an active ingredient such as anhydrous alcohol (ethanol) is slowly injected into the tissue." (Hauschild et al., col. 3, lines 31-35). There is simply no disclosure, enabling or otherwise, of a solid or semi-solid dosage form comprised of a chemical ablating agent and a biodisintegrable binder.

Similarly, Escandon et al. teaches a surgical device for the injection of liquid ethanol into the prostate ("injection of ethanol (absolute alcohol) into the prostate to be treated") (Escandon et al., col. 6, lines 58-61). Escandon et al. recommends a commercially available surgical device, the PROSTAJECT, for "chemically ablating prostate tissue by ethanol injection." (Escandon et al. col. 7, lines 9-25). As an improvement upon other injection solutions, Escandon et al. teaches "coadministering a therapeutically effective amount of an antiandrogen" with the ethanol." (Escandon et al., col. 21, lines 9-11). There is no disclosure, enabling or otherwise, of a solid or semi-solid dosage form comprised of a chemical ablating agent and a biodisintegrable binder.

Unger I and Unger II, the cited secondary references, do not remedy the deficiencies of Hauschild et al. and Escandon et al.

Unger I is directed to methods for preparing "gas-filled liposomes" for use in ultrasonic imaging applications. (Unger I, col. 1, lines 21-25). There is no disclosure of injectable or insertable dosage forms of any type, whether for chemical ablation or for any other purpose. Unger II is directed to "gas filled lipid-containing microspheres comprising at

least 50% gas in the interior thereof and an effective amount of a therapeutic agent." (Unger II, claim 1). The Examiner asserts that Unger II teaches the incorporation of ethanol for use in microsphere formulations. Even if this were assumed to be true for the sake of argument, there is simply no showing, either in Unger II or by the Examiner, that the liquid injections of ethanol of Hauschild et al. or Escandon et al. can be combined with the gas-filled lipid-containing micropheres of Unger II, and such microsphere modified to result in the solid or semi-solid dosage forms of the present invention. Based on the cited references, the Examiner has also failed to explain why there would have been a reasonable expectation of success of producing the claimed medical articles from these teachings. *See* MPEP § 2143.02 and the cases cited therein.

Not only is there a lack of explicit teaching of the combination, there is simply no motivation for one of ordinary skill to combine these references. None of the references provides a reason or suggestion to combine the references to arrive at the present invention. In re Nilssen, 851 F2d. 1401, 1403, 7 USPQ2d 1500, 1502 (Fed. Cir. 1988). Rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *In re Kahn,* 441 F.3d 977, 988 (Fed. Cir. 2006), *cited with approval in, KSR Int'l v. Teleflex, Inc.*, 127 S. Ct. 1727, 1740-41, 82 USPQ 1385, 1396 (2007). Applicants submit that the Examiner has failed to articulate a rational basis for why a person of skill in the art would combine the references in the manner indicated.

Thus, to make such a combination and make a conclusion of obviousness could only be based on the use of undue hindsight, which has long been held to be impermissible. See, for example, *Akso N.V. v. U.S. International Trade Commission*, 808 F.2d 1241, 1480-81, 1 U.S.P.Q.2d, 1241, 1246 (Fed. Cir. 1986), *cert. denied,* 482 U.S. 909 (1987); *Loctite Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 874, 228 U.S.P.Q. 90-99 (Fed. Cir. 1985).

Given the above remarks and the amendments to the claims, Applicant states that the Examiner's rejection under 35 U.S.C § 103(a) has been obviated and Applicant respectfully requests that the Examiner withdraw the rejections.

Rejection Under 35 U.S.C. § 103(a)

Claims 3, 4, and 7 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,905,475 (Hauschild et al.) and U.S. Patent No. 7,015,253 (Escandon et al.), as applied to claims 2-4 and 7-21 above, and further in view of U.S. Patent Nos. 5,770,222 (Unger III), 6443898 (Unger IV) and 6123923 (Unger V).

Applicants respectfully traverse the rejection and reiterates the arguments above with respect to Hauschild et al. and Escandon et al. There is nothing provided in Unger III, Unger IV, or Unger V, which overcomes the deficiencies noted above in order to satisfy the Examiner's burden of establishing a *prima facie* case of obviousness.

In light of the above remarks, Applicants state that the rejection under 103(a) has been obviated and all outstanding issues have been resolved. Thus, reconsideration and withdrawal of this rejection under 35 U.S.C. 103(a) is respectfully requested.

CONCLUSION

Applicants respectfully submit that all pending claims are in condition for allowance, early notification of which is earnestly solicited. Should the Examiner be of the view that an interview would expedite the application at large, request is made that the Examiner telephone the undersigned attorney at (908) 518-7700, ext. 7 in order to resolve any outstanding issues.

FEES

The Office is authorized to charge any fees required, including the fee for a three-month extension of time to deposit account number 50-1047.

Respectfully submitted,

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